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Study of Soluble Intercellular Adhesion Molecule-1 in Patients with Sepsis in Medical Intensive Care Unit, Zagazig University Hospitals and its Relation to the Clinical Outcome

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ABSTRACT

Background: Intercellular Adhesion Molecule-1 (ICAM- 1), which mediates cell-cell adhesion to the extracellular matrix, may be released in cascades throughout sepsis, causing serious damage to vascular endothelial cells. Numerous investigations have demonstrated that it is elevated in individuals with sepsis. Thus, ICAM-1 may be a useful biomarker in predicting and diagnosing sepsis.

Objectives: The aim of the current work was to measure serum sICAM-1 level in septic ICU patients to determine the association between serum sICAM-1 and inflammatory response of sepsis, clinical severity and mortality.

Patients and Methods: A Cohort study was conducted on 40 critically ill patients with sepsis and admitted to the intensive care unit in the Internal Medicine Hospital, Zagazig University Hospitals. **Results:** There was a high significant increase of SICAM-1 level in septic patients with MOF group compared to patients without MOF (p=0.003). A significant increase of serum ICAM-1 level in the non-survivors group compared to the survivor's group (p<0.001). Serum ICAM-1 had a significant positive correlation with age, APACHE II, SOFA score, TLC, ESR, CRP, urea and creatinine. There was no correlation between serum ICAM-1 with each sex, AST and ALT. Using multivariate regression analysis, it was found that serum sICAM-1 level is an independent factor for predicting the severity. Serum ICAM-1level at 232.4 ng/ml had a sensitivity of 100%, specificity of 100%, 100% NPV and 100% PPV in detecting the clinical Outcome of septic patients in ICU. **Conclusions:** It could be concluded that the increased serum level of sICAM-1 in septic ICU patients is associated with inflammatory response and organ damage and may predict their clinical Outcome during their admissions in ICU.

Keywords: Soluble Intercellular Adhesion Molecule-1, Patients with Sepsis, Medical Intensive Care unit, Clinical Outcome

INTRODUCTION

Sepsis is a global health problem caused by infection with high morbidity and mortality and is the most common cause of death in critically ill patients of intensive care units (ICU). Severe sepsis is characterized by systemic inflammatory response syndrome (SIRS) and is often complicated with septic shock (refractory hypotension) and multiple organ dysfunction syndromes (MODS), thereby determining the Outcome of severe sepsis. Both proinflammatory and anti-inflammatory pathways are activated in severe sepsis, and their imbalance can determine the probability of septic shock and MODS. Therefore, new biomarkers are highly needed in the early phase of sepsis to aid the diagnosis and stratification of severe sepsis patients [1].

Sepsis has three stages started by stage I as Systemic Inflammatory Response Syndrome (SIRS) and then stage II as severe sepsis and multiple organ dysfunction (MODS) and complicated by septic shock and death as stage III. In Egypt, the incidence rate of severe sepsis & septic shock in a study was (30.53%) with (47.13%) mortality. A gram-positive infection was evident in about one-third of the studied septic cases [2].

Intercellular adhesion molecule 1 (ICAM-1) is a glycoprotein member of the immunoglobulin superfamily and acts as one adhesion molecule that stimulates leukocyte adhesion and transmigration across the endothelium. ICAM-1 is constitutively expressed on endothelium and its expression can be significantly up-regulated by a variety of mediators, such as proinflammatory cytokines, cellular stresses, hormones and virus infection [3].

Circulating soluble ICAM-1 (sICAM-1) is cleaved and released from membrane-boundICAM-1, and measurement of blood sICAM-1 levels can estimate ICAM-1 expression in the tissue. Circulating sICAM-1 level are increased in many diseases, such as coronary heart disease, systemic lupus erythematosus, obstructive sleep apnea syndrome, atherosclerosis, idiopathic pulmonary fibrosis, colorectal and lung cancers [4].

Circulating sICAM-1 is up-regulated in neonatal sepsis and associated with disease severity and systemic inflammation. However, the relationship between circulating sICAM-1 and adult sepsis is complex and in whether sICAM-1 concentration is associated with severity and mortality of severe sepsis is not well established [5].

This study was aimed to measure serum sICAM-1 level in ICU septic patients to determine the association between serum sICAM-1 and inflammatory response of sepsis, clinical severity and mortality and to find out if sICAM-1 levels can serve as a prognostic biomarker for severe sepsis in septic patients in ICU.

PATIENTS AND METHODS

This Cohort (follow up) clinical study was conducted to explore role of serum sICAM-1 levels as a prognostic biomarker for patients with sepsis. The study included a total of 40 patients at Internal Medicine Intensive Care Units, Zagazig University Hospitals.

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Sepsis was defined as documented or suspected infection induced by a microorganism (positive blood cultures) and at least two of the following parameters: ① temperature >38°C or <36°C; ② heart rate >90 beats/min; ③ respiratory rate >20 breaths/min or $PaCO_2$ <32 mmHg; ④ white blood cell (WBC) count >12,000 or <4,000 cells/mm^3, or >10% immature forms. Severe sepsis was defined as sepsis complicated with organ dysfunction. Septic shock was defined as severe sepsis complicated with refractory arterial hypotension (SBP<90 mmHg, or MAP<65 mmHg) and fluid replacement and vasopressors were needed.

Prognosis and Outcome: Each patient was followed up till improve and discharge or die during their stay in the medical intensive care unit, internal medicine department, Zagazig University Hospitals.

Inclusion Criteria: Approval to participate on the study from the patients, critically ill patients with sepsis that admitted to intensive care unit, age more than 18 years, and Both sexes were involved.

Exclusion Criteria: Age less than 18 years, Patients not admitted to intensive care unit, critically ill patients admitted to intensive care unit without developing sepsis, and refusal to participate in the study and patients with coronary heart disease, systemic lupus erythematosus, obstructive sleep apnea syndrome, idiopathic pulmonary fibrosis, and cancers.

All patients were subjected to:

(A) Full history taking and thorough clinical examination.

(B) Routine Investigations including:

1. ***Routine laboratory investigations:*** Complete blood count (CBC), ESR, CRP, Liver function tests (AST, ALT, TP, albumin, direct and indirect bilirubin,), PT, PTT, INR, Kidney function tests (urea & creatinine), complete urine analysis, culture (blood, sputum, urine), and complete lipid profile.
2. ***Other routine investigations including:*** Chest x-ray, Abd/pelvic ultrasound, ECG, and Echocardiogram in suspected patients with infective endocarditis.

(C) Special investigation: Measure serum sICAM-1 level by ELISA (Sandwich technique). sICAM-1 levels were quantitated in baseline serum samples using the Human intercellular adhesion molecule 1(ICAM-1/CD54) ELISA Kit (SunRed)

(D) Clinical Outcome Which was Done in the first 48 hours of admission by Scoring Systems Including the Most Common Scoring System in ICU as:

1-***APACHE II scoring systems:*** Acute Physiology and Chronic Health Evaluation II is a severity-of-disease classification system [6], one of several ICU scoring systems. It is applied within 24 hours of admission of a patient to an intensive care unit (ICU): (a) Acute Physiology Score (Measured within 24 hours of admission) AaDO2 or PaO2 (for FiO2≥0.5 or <0.5, respectively). (b) Age points. (c) Chronic health points: If the patient has a history of severe organ system insufficiency: for nonoperative or emergency postoperative patients: 5 points. For elective postoperative patients: 2 points.

2-***SOFA scoring system:*** The sequential organ failure assessment score (SOFA score), previously known as the sepsis-related organ failure assessment score, is used to track a person's status during the stay in an intensive care unit (ICU) to determine the extent of a person's organ function or rate of failure [2]**.** The SOFA scoring system is useful in predicting the clinical outcomes of critically ill patients.The score tables below only describe points-giving conditions. In cases where the physiological parameters do not match any row, zero points are given. In cases where the physiological parameters match more than one row, the row with most points is picked.

***Ethical Consideration*:**

An approval of the study was obtained from Zagazig University Academic And Ethical Committee. Every patient signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Table (1) shows demographic characteristics of the study group. The age of patients ranged from 38 to 76 years with mean age ±SD being 58.21± 9.69 years and median was 59 years. Regarding gender, 23 (57.5%) patients were males while 17 (42.5%) patients were from females. The majority of patients 15 (37.5%) had hypertension followed by Diabetes Mellitus (13, 32.5%) patients then COPD (11, 27.5%).

There was high statistically significant difference between survivors and non-survivors' groups regarding age (p<0.001) but there was no statistically significant difference between the two groups regarding gender and chronic diseases.

Table (1): The demographic characteristics of the study group.

Parameters	Non-survivors (n=13)		Survivors (n=27)		p- value	Sepsis without MOF (n=18)		Sepsis with MOF (n=22)		p-value
	N	%	N	%		N	%	N	%	
Mean± SD	65.7± 6.2		54.5± 9.0		<0.001	55.0± 11.17		0.069		0.069
Male	9	69.2%	14	51.9%	0.298	8	44.4%	15	68.2%	0.131
Female	4	30.8%	13	48.1%		10	55.6%	7	31.8%	
D.M	5	38.5%	8	29.6%	0.154	9	50.0%	4	18.2%	<0.001
HTN	6	38.5%	9	33.3%		7	38.9%	8	36.4%	
Cardiac failure	4	46.2%	2	7.4%		0	0.0%	6	27.3%	
COPD	4	30.8%	7	25.9%		8	44.4%	3	13.6%	
Renal failure	6	46.2%	3	11.1%		0	0.0%	9	40.9%	
LCF, Esophageal varices	8	61.5%	6	22.2%		0	0.0%	8	36.4%	
Hyperthyroidism	0	0.0%	1	3.7%		0	0.0%	1	3.7%	

SD= standard deviation, HTN: hypertension, DM: Diabetes Mellitu, LCF: liver cell failure

There was high significant increase of serum ICAM-1 level in non-survivors group compared to survivors' group (p<0.001) (Table 2).

Table (2): Serum ICAM-1 in the study group.

Parameters		Non-survivors (n=13)	Survivors (n=27)	p- value	Sepsis with MOF (No.=22)	Sepsis without MOF (No.=18)	p- value
Serum ICAM-1 (ng/ml)	**Mean± SD**	273.6± 13.9	201.3± 20.5	<0.001	241.47± 33.41	204.59± 36.69	0.003

There was high significant increase in the levels of TLC, ESR, CRP, urea and creatinine in non-survivors compared to survivors. While there was no statistically significant difference between the both groups regarding the levels of ALT and AST (Table 3).

Table (3): Laboratory data in the study group.

Parameters		Non- survivors (n=13)	Survivors (n=27)	p- value	Sepsis without MOF (n=18)	Sepsis with MOF (n=22)	p-value
TLC (×10*9/L)	**Mean± SD**	19.7± 2.0	13.2± 3.0	<0.001	14.34± 3.13	16.06± 4.67	0.03
ESR (mm/hr)	**Mean± SD**	90.3± 5.9	25.3± .53	<0.001	40.11± 6.18	51.64± 37.99	0.796
CRP (mg/L)	**Mean± SD**	299.4± 8.8	66.4± 8.3	<0.001	93.78± 19.4	181.64± 118.65	0.003
Urea (mg/dL)	**Mean± SD**	76.1± 5.5	32.3± 6.8	.002	23.77± 4.61	65.14± 47.81	0.002
Creatinine (mg/dL)	**Mean± SD**	4.5± 1.2	1.8± 0.1	.001	1.16± 0.46	3.98± 3.24	<0.001
AST (IU/L)	**Mean± SD**	55.9± 8.8	72.0± 9.4	.761	22.61± 5.88	102.87± 92.2	0.001
ALT (IU/L)	**Mean± SD**	59.1± 8.3	65.0± 9.0	.707	23.80± 5.75	95.27± 50.2	0.010

Table (**4**) shows Scoring system in the study patients. The mean score of APACHE II in our patients was 20.8± 2.1 with median was 20 while the mean SOFA score was 11.7± 1.4 with median was 11.5. There was high statistically significant increased APACHE II and SOFA scores in non-survivors compared to survivors (p<0.001).

Table (4): Scoring system in the study patients.

Parameters		Non- survivors (n=13)	Survivors (n=27)	p- value	Sepsis without MOF (n=18)	Sepsis with MOF (n=22)	p- value
APACHE II	**Mean± SD**	23.3± 1.3	19.5±1.0	<0.001	19.33± 1.28	21.91± 1.95	<0.001
SOFA score	**Mean± SD**	13.2± 0.7	10.9±0.9	<0.001	11.28± 1.27	11.95± 1.43	0.129

Table (5) illustrates multivariate regression analysis for factors predicting severe sepsis in MOF and non- MOF cases. It was noticed that the most important factors significantly predicting severe sepsis was found to be SICAM-1 (p=0.002), AST (p=0.007) and ALT (p=0.030). While APACHE II, SOFA score, TLC, ESR, CRP, urea and creatinine were not associated and cannot act as predictors for severe sepsis.

Also, this table demonstrates multivariate regression analysis for factors predicting severe sepsis in survivor and non- survivor cases. It was noticed that the most important factor significantly predicting severe sepsis was found to be SICAM-1 (p<0.001), SOFA score (p=0.029), and CRP (p=0.029). While APACHE II, TLC, ESR, urea, creatinine, AST and ALT were not associated and cannot act as predictors for severe sepsis.

Table (5): Multivariate regression analysis for factors predicting severe sepsis between all groups.

	MOF and non- MOF groups					**Survivor and non- survivor groups**				
	Unstandardized Coefficients		**Standardized Coefficients Beta**	**t**	**p- value**	**Unstandardized Coefficients**		**Standardized Coefficients Beta**	**t**	**p- value**
	B	**Standard error**				**B**	**Standard error**			
APACHE II	.098	.057	.411	1.709	.099	.040	.024	.176	1.624	.116
SOFA	.011	.069	.032	.167	.869	.068	.029	.199	2.302	**.029**
TLC (×10*9/L)	-.011-	.022	-.087-	-.489-	.629	.011	.009	.098	1.230	.229
ESR (mm/hr)	-.007-	.004	-.527-	-2.018-	.053	.002	.002	.119	1.009	.321
CRP (mg/L)	.001	.001	.326	1.282	.210	.001	.000	.264	2.306	**.029**
Urea (mg/dL)	.000	.003	-.038-	-.160-	.874	.000	.001	.022	.200	.843
Creatinine (mg/dL)	.079	.041	.444	1.929	.064	.013	.018	.076	.739	.466
AST (IU/L)	.009	.003	1.579	2.889	**.007**	.000	.001	.022	.089	.930
ALT (IU/L)	-.008-	.004	-1.304-	-2.291-	**.030**	.000	.002	-.023-	-.090-	.929
SICAM-1 (ng/ml)	.006	.002	.474	3.275	**.002**	.011	.001	.883	11.440	**<0.001**

As shown in table (6), serum ICAM-1 had significant positive correlation with age (p=0.001), APACHE II (p< 0.001), SOFA score (p= 0.001), TLC (p< 0.001), ESR (p< 0.001), CRP (p< 0.001), urea (p= 0.004) and creatinine (p= 0.001). There was no correlation between serum ICAM-1 with sex (p= 0.657), AST (p= 0.477) or ALT (p= 0.994).

Table (6): Correlation between serum ICAM-1 and other variables in sepsis patients.

	Serum ICAM-1	
	r	**P-value**
Age (years)	.536	**0.001**
Sex	-.074	0.657
APACHE II	.819	**<0.001**
SOFA	.494	**0.001**
TLC ×10*9/L	.760	**<0.001**
ESR (mm/hr)	.565	**<0.001**
CRP (mg/L)	.666	**<0.001**
Urea (mg/dL)	.455	**0.004**
Creatinine (mg/dL)	.495	**0.001**
AST (IU/L)	.117	0.477
ALT (IU/L)	.001	0.994

** p≤0.05 is considered statistically significant, analysis done by Spearman correlation.*

Table (7) shows that serum ICAM-1 at 232.4 ng/ml or more had sensitivity of 100% and specificity of 100% in detecting Outcome in sepsis patients. The NPV and PPV was 100% and 100% respectively.

Table (7): Validity of serum ICAM-1 in prognosis and detecting outcome in sepsis patients.

	AUC	P-value	Cut off	Sensitivity	Specificity	PPV	NPV
Serum ICAM-1	1.00	<0.001	232.4 ng/ml	100%	100%	100%	100%

NPV= negative predictive value, PPV= positive predictive value

DISCUSSION

In the current study, the total number of examined patients was 40; the age of patients ranged from 38 to 76 years, with mean age ±SD being 58.21± 9.69 years and the median was 59 years. Regarding gender, 23 (57.5%) patients were males, while 17 (42.5%) patients were females. The majority of patients, 15 (37.5%), had hypertension followed by Diabetes Mellitus (13, 32.5%) patients then COPD (11, 27.5%).

There was a high statistically significant difference between survivors and non-survivor's groups regarding age. Still, there was no statistically significant difference between the two groups regarding gender and chronic diseases.

Our basic patients' demographics were closely related to another study which was conducted to determine if serum levels of endothelial adhesion molecules were associated with the development of multiple organ failure (MOF) and in-hospital mortality in adult patients with severe sepsis [7]. In this study, forty-eight patients were enrolled, of which 29 (60%) developed MOF. Patients that developed MOF had higher levels of ICAM-1; such findings revealed that high levels of serum ICAM-1 were associated with the development of MOF.

Moving to the point of sICAM-1 Levels in severe sepsis patients, our findings showed higher levels in non-survivors compared with survivors, and higher in the presence of septic shock, hypertension, diabetes mellitus, and COPD. sICAM-1 levels were shown to be highly associated with clinical severity as well as inflammatory mediator concentrations. Earlier, elevated sICAM-1 levels were seen in neonatal and adult septic patients [8]**;** our study, on the other hand, demonstrated a correlation between serum sICAM-1 and mortality in severe septic patients.

Our findings confirmed those of **Linda *et al.*** [9] who reported that in sepsis patients, blood serum concentrations of the biomarker intercellular adhesion molecule-1 (ICAM-1) elevated after seven days, suggesting that it may be a useful biomarker for assessing the severity of sepsis. Additionally, all patients who died had much greater ICAM-1 levels than those who lived.

sICAM-1 levels have already been found to be increased in diseases besides sepsis [10]**.** Although the role of sICAM-1 in sepsis is unknown, it could share similar pathways with other conditions characterized by increased sICAM-1 levels. ICAM-1 is primarily expressed on the surface of endothelial cells, and its level increases in response to tissue damage, inflammation, cellular stress, viral infection, and environmental stimuli. ICAM-1 is involved in leukocyte adhesion and migration into the subendothelial region [11].

Serum sICAM-1 concentrations were reported to be elevated in newborn infections, SIRS, sepsis-induced multiple organ failure, as well as acute trauma-induced organ failure [12]. The serum sICAM-1 is discharged from the surface of endothelial cells and serves as an excellent indication of tissue ICAM-1 levels, as demonstrated by the strong positive association between supernatant sICAM-1 and surface-bound ICAM-1 in cultured human umbilical vein endothelial cells (HUVEC) [13]**.**

sICAM-1 is a biomarker of endothelial activation, and its increased level has been shown to correlate with an increased risk of developing sepsis. In severe sepsis, infection activates and permeabilizes microvascular endothelial cells, resulting in multiple organ dysfunction. In severe sepsis, endothelial activation and dysfunction promote the progression of multiple organ failure and mortality [14]. Moving to another point, our results confirmed that levels of TLC, ESR, CRP, urea, and creatinine in nonsurvivors were higher than their levels in survivors of severe sepsis patients. At the same time, there was no statistically significant difference between both groups regarding the levels of ALT and AST.

Regarding this point, our findings are compatible with the findings of **Mira *et al.*** [15] who conducted a study to evaluate the role of ESR, TLC, and CRP in the diagnosis of sepsis in children and concluded that CRP emerged as the test with the highest sensitivity. At the same time, ESR and TLC had the highest specificity.

Another study conducted by **Ruan *et al.*** [16] concluded that CRP was observed to be a sensitive and dependable indicator of sepsis.

Numerous inflammatory biomarkers have been employed to assist in determining the clinical severity of infection. CRP, as well as TLC, are two of the most commonly used economic indicators for such purposes. CRP is indeed an acute-phase protein generated mostly by the liver in response to inflammation and infection that serves as an excellent biomarker of infection [17]**.**

CRP levels increase within 4–6 hours of damage, reach a peak within 24–48 hours, and afterward dramatically decrease as the inflammation diminishes. Due to CRP's fast increase and decrease, it is a more sensitive biomarker than WBC. CRP exhibited a strong association with clinical severity of infection, which is consistent with previous research [18]. For the last 95 years, total and differential leukocyte counts have been utilized to aid in the evaluation of infectious diseases. Neutrophilia as well as generalized leukocytosis, are the particular findings [19].

ESR and CRP have been recognized to be raised in inflammatory diseases, particularly infection, for a long period of time and were often employed as supplementary tests in sepsis and as a comparator for newer biomarkers [20]. Current research studies have raised questions on their efficacy owing to a lack of specificity. Although neutropenia had no effect on CRP alterations in septic patients, CRP was not a strong predictor of infection in neutropenic individuals [21]. Elevated CRP levels have been associated with an increased risk of mortality and organ failure in sepsis but were unable to predict survival when CRP trends were examined. CRP has been effectively used to diagnose sepsis initially, but its specificity decreases further later in the course as a result of chronically high levels [22]**.** CRP levels were considerably higher in sepsis caused by gram-negative bacterial infections than in sepsis caused by gram-positive infections, indicating a distinct immunomodulatory response [23].

There have been several investigations of CRP in sepsis in India. Sugitharini *et al.* found that CRP levels were significantly elevated in neonates with sepsis compared with those without [24]. While Sugitharini's study did not report sensitivity of CRP in detecting sepsis, a study comparing CRP levels in 80 pediatric septic patients in India with 30 healthy pediatric controls found that CRP had a sensitivity of 67%, specificity 97%, PPV 98%, and NPV 53%.

We discovered that elevated creatine and urea levels were associated with an increased risk of mortality in individuals with severe sepsis.

Urea is a recognized cause of death in a variety of conditions, including acute and chronic heart failure, coronary artery bypass grafts, acute pancreatitis, and bone marrow transplantation [25]. Additionally, urea is incorporated into the overall severity score for severely sick patients. Changes in creatine concentration were shown to be inversely proportional to changes in glomerular filtration rate. When glomerular filtration function declines, blood creatine levels rise, suggesting kidney injury, although this biomarker has poor sensitivity, reflecting that when they do, kidney function has been substantially impaired [26]**.**

When septic shock develops, several inflammatory factors impact the blood, which could also result in acute kidney damage and potentially acute renal failure. The levels of urea and creatinine are often used as clinical biomarkers of renal function. Brisco *et al.* also discovered a correlation between creatine and higher mortality, although there have been few studies demonstrating a correlation between creatine and the prognosis of septic shock patients [27]**.**

Our results reported that non-survivors had a significantly higher rate of diabetes mellitus and COPD compared with survivors. Septic shock is characterized by hypotension and disseminated intravascular coagulation (DIC), thereby contributing to multiple organ failure and a high mortality rate [28]. The endothelial barrier function is almost impaired in septic shock, and it is an important contributor to adverse outcomes [3]. Diabetes mellitus is a risk factor of sepsis, and sepsis-induced inflammation is exacerbated in Type 2 diabetic rats, and diabetes mellitus increased plasma proinflammatory cytokines levels and organs injury of septic rats [29].

Additionally, diabetic patients have elevated circulation sICAM-1 levels compared to healthy people, which is caused by genetic polymorphisms or stimulation of leptin production [30]. In pulmonary tissues of COPD patients, ICAM-1 gene expressions were increased, thereby making elevated serum sICAM-1 a biomarker of COPD [31].

As a result, the elevated serum sICAM-1 level in sepsis patients with COPD may originate from both pulmonary tissues and endothelium.

Moving to another point, our results showed that serum sICAM-1 of severe sepsis patients was correlated with the disease severity, namely APACHE II score and SOFA score on admission. Table 4 revealed that there was highly statistically significant increased APACHE II and SOFA scores in non-survivors compared to survivors.

Concerning the finding of this point, **Anjana** [32] conducted a study to prognosticate the patients by using two different established and defined scoring systems like SOFA and APACHE II, and to make attempt to establish early diagnosis of sepsis by using SOFA scoring in 50 critically ill patients with suspected multi-organ dysfunction admitted over a period of one year and concluded that Serial measurement of SOFA score during the first week is a very useful tool in predicting the Outcome especially on the day 3. The trend of SOFA score was progressively declining in survivors while non-survivors had a stable higher score during the first week. The APACHE II score on the day of admission, though reliable, was not very effective in predicting the mortality rate in our setup, which confirms our findings.

On the contrary, **Velissaris *et al.*** [33] conducted a study to validate Scoring systems for disease severity for leptospirosis and concluded that there was no association between SAPS II or SOFA scores and mortality, but survivors had significantly lower APACHE II scores compared to non-survivors, which mean that commonly used severity scores do not seem to be helpful in predicting mortality in severe leptospirosis.

Furthermore, our study's results demonstrated that patients with sICAM-1 $\geq$ 232.4 ng/mL showed a significantly higher mortality rate compared to patients with sICAM-1 level <232.4 ng/m. Also, serum ICAM-1 at 232.4 ng/ml or more had a sensitivity of 100% and specificity of 100% in detecting outcomes in sepsis patients. The NPV and PPV were 100% and 100%, respectively. Additionally, multivariate logistic regression analysis showed that serum sICAM-1 is an independent prognostic factor of severe sepsis, and this indicates more unknown mechanisms, other than inflammatory response and endothelial activation,

might be involved in the development and progression of severe sepsis.

CONCLUSION

It could be concluded that the potential for sICAM-1 to serve as a prognostic biomarker in sepsis patients, as well as its association with inflammatory response and organ damage. sICAM-1 serum levels are much higher in non-survivors than in survivors of severe sepsis admitted to the intensive care unit. Future research studies with a bigger sample size and a more comprehensive understanding of the processes are necessary to establish sICAM-1 as a unique prognostic biomarker for ICU patients with severe sepsis.

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